

Application No.: 09/816,839
Attorney Docket No.: TNX 00-04
Customer No.: 26839

I. FORMAL MATTERS

The Office has noted that the trademark DEIMMUNIZED™ was not capitalized.

Applicants have replaced the paragraphs affected by this change. It is noted that there is no generic terminology for the word DEIMMUNIZED™. However, a description of the methodology for creating a DEIMMUNIZED™ antibody appears at page 11, line 12.

II. Rejection Under 35 U.S.C. § 112, First Paragraph

A) Claims 1-4 and 10 have been rejected as lacking written description for inhibitors such as peptides, oligonucleotides, peptidomimetics, etc. Solely in an effort to expedite prosecution, Applicants have cancelled claims 1-18 and added new claims 19-35 to particularly and more distinctly claim the invention.

With regard to claim 3, now claim 21, Applicants respectfully traverse this rejection. Antibody technology is a mature technology with commonly practiced techniques well known to the skilled artisan. An artisan can readily determine whether a given antibody binds to the same epitope as MAb 175-62 by performing a routine competition assay. Example 1 clearly outlines how to obtain C2a antigen and how to generate antibodies that bind to C2a. The hybridoma that produces MAb 175-62 was deposited on March 22, 2000 with the ATCC and therefore will be available to the public. Example 16 of the Written Description Guidelines supports Applicants assertion that making antibodies is a routine art-recognized method and the functional characteristics of antibodies are well defined such that one of skill in the art would have recognized the spectrum of antibodies that are capable of binding C2a antigen and these were implicitly disclosed as a result of isolation of antigen C2.

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Therefore, Applicants respectfully submit that the specification provides sufficient written description for claim 21 and the rejection should not be applied to new claim 21. All other rejections are rendered moot by the cancellation of claims 1-18.

B) Claims 8 and 9 have been rejected as lacking enablement because the antibody MAb 155-62 is required to practice the invention. As the Office notes, this antibody was deposited by the Applicants with the ATCC, a recognized depository under the Budapest Treaty. Attached herewith is a verified statement in compliance with the deposit requirements as well as a copy of the deposit form received from ATCC. This rejection is rendered moot by the cancellation of claims 8-9, however, in view of these remarks; Applicants submit that this rejection should not apply to new claims 25 and 26.

III. Rejection Under 35 U.S.C. § 112, Second Paragraph

A) Claims 5-7 were rejected because "fragments" lacked antecedent basis. This rejection is rendered moot by the cancellation of claims 5-7. However, in view of the language of new claim 22, this rejection should not apply.

B) Claim 7 was rejected as indefinite because of the recitation of the term "Deimmunized™". Deimmunization is a procedure by which T-cell epitopes are removed from a non-human antibody rendering it less immunogenic upon administering to a human. This procedure is described in International Patent Application PCT/GB98/01473, as noted in the specification at Page 11. Applicants have used this term in claim 24 to denote an antibody that has undergone this form of removal of immunogenic sites. This description should be sufficient to allow one of skill in the art to

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determine the metes and bounds of the claim. Thus, this rejection should not apply to new claim 24.

IV. Rejection Under 35 U.S.C. § 102

A) Claims 1-4, 6, and 10 have been rejected as anticipated by Anderson et al. (Biochem. Soc. Trans. 1987 15(4):660-661). The Office alleges that Anderson et al. teach a monoclonal antibody that binds to C2a or the C2a portion of C2.

Although these claims have been cancelled rendering this rejection moot, Applicants submit that this rejection should not apply to new claims 19-21, 23, or 27. The Anderson reference teaches that it requires a 7 fold molar excess of antibody to C2 in order to achieve a 50% inhibition of C2 hemolytic activity. Figure 3 illustrates that the present invention antibodies are capable of inhibiting the classical pathway at a molar ratio of 1:2. Therefore, the present claims are not anticipated by the Anderson reference.

B) Claims 1-4 and 10 were rejected as anticipated by Inal et al. This rejection is rendered moot by the cancellation of these claims. This rejection should not apply to new claims 19-21 and 27 because Inal teaches a Sh-TOR protein, not an antibody.

V. Rejection Under 35 U.S.C. § 103(a)

A) Claim 7 was rejected as unpatentable over Anderson in view of Janeway et al. This rejection is rendered moot by the cancellation of claim 7. However, as discussed above, the primary reference does not teach antibodies capable of inhibition at a molar ratio of 1:2, therefore this rejection should not apply to new claim 24.

B) Claim 5 was rejected as unpatentable over Anderson in view of U.S. Pat. No. 5,861,156. This rejection is rendered moot by the cancellation of claim 5.

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However, as discussed above, the primary reference does not teach antibodies capable of inhibition at a molar ratio of 1:2, therefore this rejection should not apply to new claim 22.

CONCLUSION

In view of the foregoing amendments and remarks, Applicants submit that the claims are in condition for Allowance and request a timely Notice indicating such.

Respectfully Submitted,

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Marked Version of Substitute Paragraphs:

At Page 6, line 16:

One embodiment of the present invention includes an inhibitor molecule comprising a monoclonal antibody. The antibody may be chimeric, [Delimmunized™] DEIMMUNIZED™ (described below), humanized or human antibody. Specifically, the monoclonal antibody may be the monoclonal antibody designated 175-62.

At Page 7, line 1:

Another embodiment of the invention includes monoclonal antibodies or a fragment, analogue or homologue thereof, or a peptide, oligonucleotide, peptidomimetic or an organic compound which bind to the same epitope as the antibody 175-62. These antibodies can include Fab, F(ab')₂, Fv or single chain Fv, and may be chimeric, [Delimmunized™] , DEIMMUNIZED™ humanized or human antibody. In addition, the present invention includes cell lines that produces the monoclonal antibody or fragment thereof that bind to the same epitope as the antibody 175-62.

At Page 10, line 14:

When treating inflammatory or autoimmune diseases in humans, the anti-C2a antibodies may be chimeric, [Delimmunized™] DEIMMUNIZED™, humanized or human antibodies. Such antibodies can reduce immunogenicity, thereby avoiding a human/anti-mouse antibody (HAMA) response. It is preferable that the antibody be IgG4, IgG2, or other genetically mutated IgG or IgM which does not augment antibody-dependent cellular cytotoxicity (S.M. Canfield et al., *J. Exp. Med.*, 1991, 173: 1483-1491) and complement mediated cytosis (Y.Xu et al., *J. Biol. Chem.*, 1994, 269: 3468-3474; V.L. Pulito et al., *J. Immunol.*, 1996, 156: 2840-2850).

At Page 11, line 12:

DEIMMUNIZED™ [Delimmunized™] antibodies are antibodies in which the T-helper epitopes have been eliminated, as described in International Patent Application PCT/GB98/01473. They have either reduced or no immunogenicity when administered *in vivo*.

Example 16: Antibodies

Specification: The specification teaches that antigen X has been isolated and is useful for detection of HIV infections. The specification teaches antigen X as purified by gel filtration and provides characterization of the antigen as having a molecular weight of 55 KD. The specification also provides a clear protocol by which antigen X was isolated. The specification contemplates but does not teach in an example antibodies which specifically bind to antigen X and asserts that these antibodies can be used in immunoassays to detect HIV. The general knowledge in the art is such that antibodies are structurally well characterized. It is well known that all mammals produce antibodies and they exist in five isotypes, IgM, IgG, IgD, IgA and IgE. Antibodies contain an effector portion which is the constant region and a variable region that contains the antigen binding sites in the form of complementarity determining regions and the framework regions. The sequences of constant regions as well as the variable regions subgroups (framework regions) from a variety of species are known and published in the art. It is also well known that antibodies can be made against virtually any protein.

Claim: An isolated antibody capable of binding to antigen X.

Analysis:

A review of the full content of the specification indicates that antibodies which bind to antigen X are essential to the operation of the claimed invention. The level of skill and knowledge in the art of antibodies at the time of filing was such that production of antibodies against a well-

characterized antigen was conventional. This is a mature technology where the level of skill is high and advanced.

The claim is directed to any antibody which is capable of binding to antigen X.

A search of the prior art indicates that antigen X is novel and unobvious.

Considering the routine art-recognized method of making antibodies to fully characterized antigens, the well defined structural characteristics for the five classes of antibody, the functional characteristics of antibody binding, and the fact that the antibody technology is well developed and mature, one of skill in the art would have recognized that the spectrum of antibodies which bind to antigen X were implicitly disclosed as a result of the isolation of antigen X.

Conclusion: The disclosure meets the requirement under 35 USC 112 first paragraph as providing an adequate written description of the claimed invention.